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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,199	09/01/2006	John Brownlie	ERP02.001APC1	6472

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
12/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,199	BROWNLIE ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-19,27-34 and 38-63* is/are pending in the application.

4a) Of the above claim(s) *16-19,27-34,38,39 and 43-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 8-15, 40-42, and 57-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/19/2008* .
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 6-17-08 8-22-08. Claims 1, 8-19, 27-34, and 38-63 are pending. Claim1 has been amended. Claims 16-19, 27-34, 38-39 and 43-56 have been withdrawn. Claims 2-7, 20-26, and 35-37 have been cancelled. Claims 1, 8-15, 40-42, and 57-63 are under examination.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejection to claims 1-2, 4-7, 10-15 under 35 U.S.C. 112, is withdrawn in light of applicant's amendment and cancellation of claims.

b) Rejection to claims 1, 3, and 8 under 35 U.S.C. 102(b) as being anticipated by Mackenzie et al EP 0415794A1.

c) Rejection to claims 1, 3, and 8 under 35 U.S.C. 102(a) as being anticipated by Jira et al US 20030039667 Publication Date February 27, 2003.

d) Rejection to claims 1-3, 8-11, 40, and 42 under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Jacobs et al US Patent No. 6,682,745 and Brown et al US Patent No. 5,661,006.

e) Rejection to claims 1, 3-4 and 8 under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Hechard et al 2003 Journal of Medical Microbiology Vol. 52 pgs. 35-40.

f) Rejection to claims 1 and 3-5, 8-9, 12-13, and 41 under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Hansen et al US Patent NO: 5,665,363.

g) Rejection to claims 1, 3, 6, and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Masubuchi et al 2002 J Vet Med Sci 64(12): 1165-1168.

h) Rejection to claims 1, 3, 7, and 8 under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Marciani et al US Patent No: 6,080,725 Date 6/27/2000.

i) Rejection to claims 1, 3, and 14 under 35 U.S.C. 103(a) as being unpatentable over Mackenzie et al EP 0415794A1 in view of Haanes et al US Patent No: 5,753,235 Date 5/19/1998.

Information Disclosure Statement

3. The information disclosure statement filed on 11/19/2008 has been considered. Initialed copies are enclosed.

New Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 58 and 60-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a vast genus of immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a

particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives, applicant must also give a functional limitation of immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives.

The specification, however, does not disclose distinguishing and identifying features of a representative member of the genus of the immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives, to which the claims are drawn, such as a correlation between structure of the peptide and its recited function, so that the skilled artisan could immediately envision or recognize at least a substantial number of members of the claimed genus of immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives.

Even though one could screen for which changes in the immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives will maintain protection from infection, the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. The written description requirement is separate and distinct from the enablement requirement (See also *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir. 2004) and adequate written description requires more than a mere reference to a potential method for identifying candidate polypeptides. In such an unpredictable art, as set forth supra, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See *Noelle v Lederman*. 355 F. 3d 1343, 1350, 69 USPQ2d 1508, 1514 (*Fed. Cir. 2004*) and *In re Alonso* (Fed. Cir. 2008-1079).

The dictionary definition of vaccine is "A prophylactic or therapeutic material containing antigens derived from one or more pathogenic organisms which, on

administration to man or animal, will stimulate active immunity and protect against infection with these or related organism (i.e. produce protective immunity)." (The Dictionary of Immunology, Herbert et al eds, Academic Press, 1995).

The specification lacks written description of the instant immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives that are protective when administered. For example, Colman et al. (Research in Immunology 145: 33-36, 1994, p.33 column 2, p. 35 column 1) disclose that a single amino acid changes in an antigen can effectively abolish the interaction with an antibody entirely and that a very conservative amino acid substitution may abolish antibody binding and a non-conservative amino substitution may have little effect in antibody binding. This underlies the importance of the description of the immunoepitopes that are protective and which conservative amino acid substitutions and where and how many changes can the immunoepitopes tolerate and still retain the ability to protect from infection.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc.'v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual

reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. Additionally Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Therefore, in accordance with the Guidelines, the description of immunogenic fragments, derivatives, or nucleic acids encoding said fraction or derivatives is not deemed representative of the claimed invention thus the claim does not meet the written description requirement.

5. Claims 1, 8-15, 40-42, and 58-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for any vaccine composition for vaccinating dogs comprising an agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD). The specification is also not enabled for any vaccine composition comprising: an agent capable of raising an immune response against M. cynos in a dog; and an agent capable of raising an immune response against CRCV in a dog.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims. The claim is very broad and to any vaccine comprising for vaccinating dogs comprising any agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD) and drawn to a vaccine composition comprising: an agent capable of raising an immune response against M. cynos in a dog; and an agent capable of raising an immune response against CRCV in a dog.

The nature of the instant invention is the use of any agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD) to treat dogs. Furthermore the vaccine further comprises, one ore more agents capable of raising an immune response in a dog against canine respiratory coronavirus (CRCV); an agent capable of raising an immune response in a dog against canine parainfluenzavirus (CPIV); an agent capable of raising an immune response in a dog against canine adenovirus type 2 (CAV-2); an agent capable of raising an immune response in a dog against canine herpesvirus (CHV); an agent capable of raising an immune response in a dog against Bordetella bronchiseptica (B. bronchiseptica); an agent capable of raising an immune response against S. zooepidemicus in a dog comprises inactivated or attenuated S. zooepidemicus, or a structural protein of S. zooepidemicus or an immunogenic portion thereof, or a sequence variant of said structural protein or immunogenic portion thereof, or a nucleic acid encoding said structural protein, portion or sequence variant, wherein said sequence variant has at least 90% sequence identity to the polypeptide sequence of said structural protein or immunogenic portion thereof; an agent capable of raising an immune response against a Chlamydophila in a dog comprises inactivated or attenuated Chlamydophila, or a structural protein of Chlamydophila or an immunogenic portion thereof, or a sequence variant of said structural protein or immunogenic portion thereof, or a nucleic acid encoding said structural protein, portion or sequence variant, wherein said sequence variant has at

least 90% sequence identity to the polypeptide sequence of said structural protein or immunogenic portion thereof to treat dogs.

The teachings of the specification are limited to only the association of Streptococcus equi sub species zooepidemicus with canine infectious respiratory disease, the association of Mycoplasmas cynos with canine infectious respiratory disease, the association of Chlamydophila with canine infectious respiratory disease, the association of canine herpesvirus with canine infectious respiratory disease. The specification does not provide guidance on how to treat canine infectious respiratory disease with any agents as discussed above.

The art as at the time of filing teaches that: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.., and thus protect the host against attack by the pathogen. Furthermore, A vaccine “must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough.” In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)."

The state of the art indicates a vaccine composition against microbes such as Mycoplasma cynos such as administering an agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in an animal such as a dog (see abstract, pg. 2 lines 34-54, pg. 3 lines 15-17, pg. 4 last paragraph) (see Mackenzie et al EP 0415794A1 abstract or reference in its entirety). The state of the art teaches a method for administering a live attenuated bacterial vaccine to a mammal, comprising: injecting into a submucosal tissue of a mammal such as a dog an immunogenically

effective amount of a live attenuated bacterium, wherein said live attenuated bacterium is selected from the group consisting of Streptococcus equi and Streptococcus zooepidemicus (see Jacob et al US Patent No. 6,682,745 abstract or reference in its entirety). The art teaches an isolated and purified nucleic acid sequence encoding a polypeptide having one or more immunogenic determinants of a Canine coronavirus (CCV) spike protein, a recombinant vector or recombinant vector virus comprising such a nucleic acid sequence, a host cell transformed with such a recombinant vector or infected with the recombinant vector or infected with the recombinant vector virus which can be applied for the preparation of a vaccine for the immunization of dogs against CCV infection (see Brown et al US Patent No. 5,661,006 abstract or reference in its entirety). The art teaches that a protective effect of DNA vaccination with the gene encoding the major outer-membrane protein (MOMP) of *Chlamydophila abortus* of mice vaccinated intramuscularly three times every 3 weeks, mated and challenged with *C. abortus* elicited a specific humoral response with predominantly IgG2a antibodies (see abstract, Hechard et al 2003 Journal of Medical Microbiology Vol. 52 pgs. 35-40). The art teach that biologically active materials acts as an immunogen are Bordetella bronchiseptica, Canine adenovirus (CAV-2), Canine Parainfluenza (CPIV), and Chlamydia psittaci in a vaccine (see Hansen et al US Patent No: 5,665,363 see claims). The art teaches the investigation into the causes of canine infectious respiratory disease that indicated the presence of canine respiratory coronavirus and canine herpesvirus in two kenneled dog populations (see Erles et al Arch Virol 2005 Vol. 150 pgs. 1493-1504). The art does not teach any vaccine comprising for vaccinating dogs comprising any agent discussed above or specifically an agent capable of raising an immune response against Mycoplasma cynos (M. cynos) or and an agent capable of raising an immune response against CRCV in a dog and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD). This constitutes undue experimentation. For the reasons set forth supra, the state of the art is unpredictable to the vaccine for vaccinating dogs comprising any agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune

response is protective against Canine Infectious Respiratory Disease (CIRD) and a vaccine composition comprising: an agent capable of raising an immune response against M. cynos in a dog; and an agent capable of raising an immune response against CRCV in a dog.

Guidance in the specification. The specification fails to describe any vaccine comprising vaccine for vaccinating dogs comprising any agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD) and a vaccine composition comprising: an agent capable of raising an immune response against M. cynos in a dog; and an agent capable of raising an immune response against CRCV in a dog. There is not empirical data reported on the specification at the time of filing showing efficacy of a therapeutic agent.

Working examples. The specification does not give any working example (i.e. challenged mice models or passive immunization approaches).

In conclusion, the claimed invention are not enabled for a vaccine for vaccinating dogs comprising any agent capable of raising an immune response against Mycoplasma cynos (M. cynos) in a dog, wherein said agent comprises inactivated or attenuated M. cynos, and wherein said immune response is protective against Canine Infectious Respiratory Disease (CIRD) and a vaccine composition comprising: an agent capable of raising an immune response against M. cynos in a dog; and an agent capable of raising an immune response against CRCV in a dog. The specification fails how to treat Canine Infectious Respiratory Disease (CIRD) with any agents as set forth supra for dogs. In view of the lack of support in the art and specification for the claimed invention as set forth supra, it would require undue experimentation on the part of the skilled artisan to use the vaccine as claimed; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed method.

Status of the Claims

6. No claims are allowed.

Claims 1, 8-15, 40-42, and 57-63 are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. A. A./

Examiner, Art Unit 1645

Nina A Archie

Examiner

GAU 1645

REM 3B31

/Mark Navarro/

Primary Examiner, Art Unit 1645